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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/943,722 | 08/31/2001 | George N. Pavlakis | 2026-4006US5 | 2624 |

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[REDACTED] EXAMINER

SIEW, JEFFREY

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1637 | 10 |

DATE MAILED: 10/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|--------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/943,722 | PAVLAKIS ET AL. |
| | Examiner Jeffrey Siew | Art Unit 1656 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 09 August 2002.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,2,6-20,22,25-29,31-33 and 46-49 is/are pending in the application.
- 4a) Of the above claim(s) 1,2,6-20,22,25-29 and 31-33 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 46-49 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 8/31/01 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>4 . 7 pages</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The cancellation of claims 3-5,21,23,24,30,34-45 on August 31, 2001 has been acknowledged and entered. The restriction filed 7/9/02 is still maintained over the remaining pending claims. It is also noted in the response filed 8/31/01 page 6 the response refers to new claims 73-76 but such claims are not pending. It has been inferred that the claims referred to new claims 46-49.

Election/Restrictions

2. Claims 1,2,6-20,22,25-29 and 31-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No.9 .

Priority

3. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. **If a parent application has become a patent,**

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the expression “now Patent No. _____” should follow the filing date of the parent application. If a parent application has become abandoned, the expression “now abandoned” should follow the filing date of the parent application.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Specification

4. In Figure 1 second sheet should be labeled “Figure 1 continued”. In Figure 14 second, third and fourth sheet should be labeled “Figure 14 continued”.

Figures 13 & 14B should be identified by proper SEQ ID NO.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 46- 49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No.6,414,132 in view of Coulombe et al (Gene vol. 46 pp 89-95 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 46-48 are drawn to any **synthetic gene** with less preferred codons replaced by preferred codon and expression in mammalian cells. Claim 49 is drawn to the **method of making** the synthetic gene.

Claims 1-12 of US 6,414,132 are drawn to a **method of making** a gene by substituting **less preferred codons with more preferred codon** and introducing into a eukaryotic cell, culturing and expression (see in particular claim 1,6,9 & 12).

Claims 1-12 of US 6,414,132 are **not** drawn to a **mammalian expression**.

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Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells**, a form of mammalian expression. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 1-12 of US 6,414,132 in order to produce the recombinant protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion). It would have been prima facie obvious to apply Coulomb et al's mammalian expression which were well known at the time the invention was made to the claimed method of substituting preferred codons in order to abundantly express mammalian proteins for analysis.

Moreover, as the method of producing the synthetic gene would obviously result in the product claims 46-48 which are drawn to synthetic gene with less preferred codon replaced by preferred codon. It would have been prima facie obvious that one of ordinary skill in the art would apply Coulombe et al's mammalian expression system to the method claims 1-12 of US6,414,132 in order to produce the recombinant product for analysis, inevitably resulting in the claimed synthetic gene.

.5. Claims 46- 48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-12 of U.S. Patent No. 6,291,664 in view of Coulombe et al (Gene vol. 46 pp 89-95 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 46-48 are drawn to any **synthetic gene** with less preferred codons replaced by preferred codon and **expression in mammalian cells**.

Claims 3-12 & 33 of US 6,291,664 are drawn to **HIV env gene construct** with substituted less preferred codons with more preferred codon (e.g. see claim 3 SEQ ID NO:102 c substituted for wild type T at position 6686) and introducing into a vector and cell for expression.

Claims 3-12 & 33 of US 6,291,664 are **not** drawn to any **expression in mammalian cell system**.

Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells**, a form of **mammalian expression**. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 3-12 & 33 of US 6,291,664 in order to produce the recombinant env protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion). It would have been prima facie obvious to apply Coulomb et al's mammalian expression which were well known at the time the invention was made to the claimed method of substituting preferred codons in order to abundantly express mammalian proteins for analysis.

Moreover, as claims 3-12 & 33 of US 6,291,664 which are drawn to **HIV env gene**, represent a species of the genus claims 46-48 of the instant application which are drawn to any synthetic gene. The species would render the genus obvious.

6. Claims 46-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-6 of U.S. Patent No. 5,965,726 in view of Coulombe et al (Gene vol. 46 pp 89-95 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 46-48 are drawn to any **synthetic gene** with less preferred codons replaced by preferred codon and **expression in mammalian cells**.

Claims 3-6 of US 5,965,726 are drawn to composition comprising a **HIV gag gene nucleic acid construct** with silent substituted **less preferred codons with more preferred codon** (e.g. see claim 3 SEQ ID NO:6 c substituted for wild type T at position 422 & Figure 4).

Claims 3-6 of US 5,965,726 are **not** drawn to any expression in **mammalian cell system**.

Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells**, a form of mammalian expression. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 3-6 of US 5,965,726 in order to produce the recombinant gag protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion). It would have been prima facie obvious to apply Coulomb et al's mammalian expression which were well known at the time the invention was made to the claimed method of substituting preferred codons in order to abundantly express mammalian proteins for analysis.

Moreover, as claims 3-6 of US 5,965,726 represent a species of HIV gag construct with silent substitution to produce a more preferred codon of the genus claims 46-49 of the instant claim which are drawn to any synthetic gene expressed in an eukaryotic cell with less preferred codon replaced by preferred codon. The species would render the genus obvious.

7. Claims 46-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,972,596 in view of Coulombe et al (Gene vol. 46 pp 89-95 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 46-48 are drawn to **any synthetic gene** with less preferred codons replaced by preferred codon and **expression in mammalian cells**.

Claims 1-10 of U.S. Patent No. 5,972,596 are drawn to a **HIV gag nucleic acid construct** with silent substituted less preferred codons with more preferred codon (e.g. see claim 1 SEQ ID NO:6 c substituted for wild type T at position 422 & Figure 4).

Claims 1-10 of U.S. Patent No. 5,972,596 are not drawn to any expression in **mammalian cell system**.

Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells**, a form of mammalian expression. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 1-10 of U.S. Patent No. 5,972,596 in

order to produce the recombinant gag protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion).

Moreover, as claims 1-10 of U.S. Patent No. 5,972,596 which are drawn to **HIV gag gene**, represent a species of the genus claims 46-48 of the instant application which are drawn to any synthetic gene. The species would render the genus obvious.

8. Claims 46-49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,174,666 in view of Coulombe.

Claims 46-48 are drawn to any **synthetic gene** with less preferred codons replaced by preferred codon and expression in mammalian cells. Claim 49 is drawn to the **method of making** the synthetic gene. 1-9 of U.S. Patent No. 6,174,666

Claims 1-9 of U.S. Patent No. 6,174,666 are drawn to a **method of making** a gene by substituting **less preferred codons with more preferred codon** and introducing into a eukaryotic cell, culturing and expression (see in particular claim 1,6,9 & 12).

Claims 1-9 of U.S. Patent No. 6,174,666 are not drawn to a **mammalian expression**.

Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells**, a form of mammalian expression. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 1-9 of U.S. Patent No. 6,174,666 in order

to produce the recombinant protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion). It would have been prima facie obvious to apply Coulomb et al's mammalian expression which were well known at the time the invention was made to the claimed method of substituting preferred codons in order to abundantly express mammalian proteins for analysis.

Moreover, as the method of producing the synthetic gene would obviously result in the product claims 46-48 which are drawn to synthetic gene with less preferred codon replaced by preferred codon. It would have been prima facie obvious that one of ordinary skill in the art would apply Coulombe et al's mammalian expression system to the method claims 1-12 of US6,414,132 in order to produce the recombinant product for analysis, inevitably resulting in the claimed synthetic gene.

9. Regarding the above double patenting rejections, the response is also guided to MPEP 804 one way obviousness. If the application at issue is the later filed application or both are filed on the same day, only one-way determination of obviousness is needed in resolving the issue of double patenting (MPEP 800-23).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 46-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Clarke et al (US4,959,455 September 25, 1990).

Clarke et al teach the method of constructing a synthetic gene and synthetic gene of primate IL-3 into a vector by recombinant techniques (see whole doc. esp. abstract). They teach a synthetic gene encoding IL-3 which is normally expressed in eukaryotic cells (see col. 1 line 19, line 60-65 & col. 9 lines 58-65)). They teach replacing a less preferred codon for a more preferred codon in both bacterial and mammalian systems (see col. 9 lines 67-col. 10 lines 12 & Table III). They teach insertion of synthetic gene in a vector(see col. 10 line12). They teach the transfection into COS for mammalian cell expression system (see col. 11 line 57-68).

SUMMARY

11. No claims allowed.

CONCLUSION

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is Jeffrey.Siew@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The

examiner is on flex-time schedule and can best be reached on weekdays from 6:30 a.m. to 3 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119.

Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Monica Graves for Art Unit 1637 whose telephone number is (703)-306-2938.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-3290 and Before Final FAX (703) 872-9306 or After Final FAX (703) 30872-9307.

Jeffrey Siew
JEFFREY SIEW
PRIMARY EXAMINER

October 19, 2002